*There is growing attention and concern about the association of antipsychotic medications, obesity, and diabetes mellitus. Linked to the increase in obesity and the prevalence of diabetes, along with the inadequacy of prevention and health care for the chronically mentally ill, the use of these agents is becoming a major public health issue and has a great economic impact. Last November, the American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for the Study of Obesity convened a consensus development conference on this topic. The resulting consensus statement appears in the February 2004 issue of Diabetes Care (2004;27:596–601). It is extraordinarily rare for us to agree to dual publication, but because we believe this topic is of great concern to clinical psychiatrists, the* Journal *has accepted exclusive rights to bring this important information to psychiatrists in this month's issue. —AJG*

# Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes


AMERICAN DIABETES ASSOCIATION
AMERICAN PSYCHIATRIC ASSOCIATION
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
NORTH AMERICAN ASSOCIATION FOR THE STUDY OF OBESITY


Antipsychotic medications are an important component in the medical management of many psychotic conditions. With the introduction of the second-generation antipsychotics (SGAs) over the last decade, the use of these medications has soared. Although the SGAs have many notable benefits compared with their earlier counterparts, their use has been associated with reports of dramatic weight gain, diabetes (even acute metabolic decompensation, e.g., diabetic ketoacidosis [DKA]), and an atherogenic lipid profile (increased LDL cholesterol and triglyceride levels and decreased HDL cholesterol).

Because of the close associations between obesity, diabetes, and dyslipidemia and cardiovascular disease (CVD), there is heightened interest in the relationship between the SGAs and the development of these major CVD risk factors. To gain a better understanding of this relationship, the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity convened a consensus development conference 19–21 November 2003 on the subject of antipsychotic drugs and diabetes. An eight-member panel heard presentations from 14 experts drawn from the areas of psychiatry, obesity, and diabetes. Presentations were also made by a representative from the U.S. Food and Drug Administration (FDA) and by representatives from the AstraZeneca, Bristol-Myers Squibb, Janssen, Lilly, and Pfizer pharmaceutical companies. In addition, before the conference, the consensus panel was given copies of most of the known peer-reviewed, English language clinical studies published in this area, as well as additional articles from animal studies; other papers and abstracts were reviewed at the conference.

With this information, the panel developed a consensus position on the following questions:

1. What is the current use of antipsychotic drugs?
2. What is the prevalence of obesity, prediabetes, and type 2 diabetes in the populations in which the SGAs are used?
3. What is the relationship between the use of these drugs and the incidence of obesity or diabetes?
4. Given the above risks, how should patients be monitored for the development of significant weight gain, dyslipedemia, and diabetes, and how should they be treated if diabetes develops?
5. What research is needed to better understand the relationship between these drugs and significant weight gain, dyslipedemia, and diabetes?

## 1. WHAT IS THE CURRENT USE OF ANTIPSYCHOTIC DRUGS?

Antipsychotic medications (Table 1) are the mainstay of treatment for psychotic illnesses and are also widely used in many other psychiatric conditions. Introduced ~50 years ago, these medications have helped millions of people manage their symptoms. For people who respond well, antipsychotics can mean the difference between leading an engaged, fulfilling community life and being severely disabled.

The first-generation antipsychotics (FGAs) are still widely available and are effective at treating positive symptoms of psychosis, such as hallucinations and delusions. FGAs do not, however, adequately alleviate many other common and important aspects of psychotic illness, such as negative symptoms (e.g., withdrawal, apathy, poverty of speech), cognitive impairment, and affective symptoms. In addition, all FGAs can produce significant extrapyramidal side effects at clinically effective doses. These side effects, which include dystonic reactions, drug-induced parkinsonism, akathisia, and tardive dyskinesia, can make treatment intolerable for some people, leading to subjective distress, diminished function, stigma, and nonadherence.

The effort to find more effective medications with fewer and less-severe side effects led to the development of the SGAs, often referred to as the "atypical antipsychotics." SGAs have fewer or no extrapyramidal side effects at clinically effective doses. Many of these newer medications are also more effective than the older agents at treating the negative, cognitive, and affective symptoms of psychotic illnesses.

The six currently available SGAs vary in their efficacy, formulation, biochemistry, receptor binding, and side effect profiles. One of them, clozapine, is clearly the most effective antipsychotic. However, clozapine is only indicated after other medications have failed or in patients at high risk for suicidal behavior, largely because it can cause agranulocystosis.

In general, SGAs are better tolerated and more effective than the FGAs. Aside from clozapine, they have become the first-line agents for their indicated use and


*From the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity.*


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*Abbreviations: CVD, cardiovascular disease; DKA, diabetic ketoacidosis; FDA, Food and Drug Administration; FGAs, first-generation antipsychotics; SGAs, second-generation antipsychotics.*

**Table 1.**
**Antipsychotic Medications**

| | Generic name | Trade name | Year approved |
|---|---|---|---|
| Commonly used FGAs | Chlorpromazine | Thorazine | — |
| | Perphenazine | Trilafon | — |
| | Trifluoperazine | Stelazine | — |
| | Thiothixene | Navane | — |
| | Haloperidol | Haldol | — |
| | Fluphenazine | Prolixin | — |
| SGAs | Clozapine | Clozaril | 1989 |
| | Risperidone | Risperdal | 1993 |
| | Olanzapine | Zyprexa | 1996 |
| | Quetiapine | Seroquel | 1997 |
| | Ziprasidone | Geodon | 2001 |
| | Aripiprazole | Abilify | 2002 |

are increasingly being used off-label. In current practice, people who are likely to be treated with an SGA include those with schizophrenia spectrum disorders, bipolar disorder, dementia, psychotic depression, autism, and developmental disorders and, to a lesser extent, individuals with conditions such as delirium, aggressive behavior, personality disorders, and posttraumatic stress disorder. These psychiatric conditions are common and often require lifelong treatment. In the U.S., the prevalence of schizophrenia and related conditions is ~ 1%, the prevalence of bipolar disorders is ~ 2%, and the prevalence of major depression is ~ 8%. The SGAs are therefore widely used medications, and their use has important public health ramifications.

## 2. WHAT IS THE PREVALENCE OF OBESITY, PRE-DIABETES, AND TYPE 2 DIABETES IN THE POPULATIONS IN WHICH THE SGAs ARE USED?

It is difficult to determine whether the prevalence of these metabolic disorders is increased in these psychiatric populations independent of drug treatment. Most of the available data are derived from studies of individuals with schizophrenia, and even in this condition, the evidence is very limited. Data from most studies suggest that the prevalence of both diabetes and obesity among individuals with schizophrenia and affective disorders is ~1.5–2.0 times higher than in the general population. Many characteristics of people with schizophrenia, such as sedentary behavior, may contribute to the apparently higher prevalence of metabolic abnormalities. However, none of these studies controlled for all of the major diabetes risk factors. For example, BMI and family history of diabetes were rarely determined, nor were the control populations appropriately matched for these and other variables. Thus, it is unclear whether psychiatric conditions per se, independent of other known diabetes risk factors, account for the increased prevalence.

There are limited data evaluating the metabolic profile and diabetes risk of drug-naïve subjects with schizophrenia. In a small cohort of adults with schizophrenia untreated with medications, visceral fat content (which is correlated with insulin resistance) was threefold higher than in age- and BMI-matched control subjects. In another study, the same investigators found that drug-naïve patients presenting with their first episode of schizophrenia had an increased prevalence of impaired fasting glucose, were more insulin resistant, and had higher plasma levels of glucose, insulin, and cortisol than did matched control subjects.

Overall, the limited amount of epidemiological data suggest an increased prevalence of obesity, impaired glucose tolerance, and type 2 diabetes in people with psychiatric illness. Whether this is a function of the illness itself versus its treatment is unknown. Studies using the proper diagnoses of glucose intolerance and more complete risk factor characterization are necessary in order to resolve this issue.

## 3. WHAT IS THE RELATIONSHIP BETWEEN THE USE OF THESE DRUGS AND THE INCIDENCE OF OBESITY OR DIABETES?

Recognition of an association between SGAs and diabetes was first derived from case reports of severe, sometimes fatal, acute diabetic decompensation, including DKA. Subsequent drug surveillance and retrospective database analyses suggest there is an association between specific SGAs and both diabetes and obesity. This potential relationship is of considerable clinical concern because obesity and diabetes are important risk factors for CVD, and the relative risk of CVD mortality is significantly greater in people with psychiatric disorders than in the general population. High rates of smoking and physical inactivity may also contribute to the excess mortality. Therefore, if SGA therapy further increases the risk for obesity and type 2 diabetes, this should be of major clinical concern.

Although there are significant shortcomings in many of the studies examining the relationships between the SGAs and obesity or diabetes, clear-cut trends can be identified.

### Obesity

There is considerable evidence, particularly in patients with schizophrenia, that treatment with SGAs can cause a rapid increase in body weight in the first few months of therapy that may not reach a plateau even after 1 year of treatment. There is, however, considerable variability in weight gain among the various SGAs (Table 2). At 10 weeks of therapy, estimated average weight gain with drug treatment compared with placebo varies from ~0.5 to 5.0 kg. Limited data suggest that in humans, most of the weight gained

**Table 2.**
**SGA's and Metabolic Abnormalities**

| Drug | Weight gain | Risk for diabetes | Worsening lipid profile |
|---|---|---|---|
| Clozapine | +++ | + | + |
| Olanzapine | +++ | + | + |
| Risperidone | ++ | D | D |
| Quetiapine | ++ | D | D |
| Aripiprazole* | +/− | − | − |
| Ziprasidone* | +/− | − | − |

+ = increase effect; − = no effect; D = discrepant results. *Newer drugs with limited long-term data.



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is fat. Data derived from a canine model indicated that certain SGAs increase total visceral fat mass and intrahepatic lipid content.

The mechanism(s) responsible for weight gain associated with SGA therapy are unknown. Weight gain occurs when more energy is ingested than is expended. Therefore, weight gain is due to increased energy intake, decreased energy expenditure, or both. Even a small, chronic imbalance between energy intake and expenditure can lead to large changes in body weight over time. For example, ingestion of ~500 kcal/day more than is expended can account for the largest average weight gain reported with SGA therapy (4.5 kg at 10 weeks). This amount of daily increase in energy intake represents the calories in a normal-size candy bar plus a soda or in an ice cream dessert. Hunger and satiety may be altered in people taking SGAs because of the known binding affinities of these drugs to serotonin, norepinephrine, dopamine, and particularly histamine-H1 receptors. All of these receptors have been implicated in the control of body weight.

Weight gain and changes in body composition may account for many of the purported metabolic complications associated with SGA therapy, e.g., insulin resistance, pre-diabetes, diabetes, and dyslipidemia. A possible direct effect of SGAs on β-cell function and insulin action in liver and muscle tissue could also be involved, as discussed below.

### Diabetes

Numerous case reports have documented the onset or exacerbation of diabetes, including the occurrence of hyperglycemic crises, following initiation of therapy with many of the SGAs.

Several of these events occurred within a few weeks of initiating drug treatment. In some, but not all cases, hyperglycemia promptly resolved after the medication was discontinued. Several reports documented recurrent hyperglycemia after another challenge with the same drug. Additional cases of diabetes or hyperglycemia have been reported through MedWatch into the FDA's Adverse Event Reporting System.

Large retrospective cohort studies have been reported that estimate the prevalence of diabetes in patients using SGAs. These reports relied on a variety of methods for determining the diagnosis of diabetes, such as ICD-9 codes and data on prescriptions for diabetes medications. In addition, several cross-sectional studies of patients taking different SGAs, "switch studies" of patients changed from one medication to another, and one prospective randomized controlled trial evaluating SGA therapy on parameters of insulin sensitivity and glycemic control have been conducted. Despite limitations in study design, the data consistently show an increased risk for diabetes in patients treated with clozapine or olanzapine compared with patients not receiving treatment with FGAs or with other SGAs. The risk in patients taking risperidone and quetiapine is less clear; some studies show an increased risk for diabetes, while others do not. The two most recently approved SGAs, aripiprazole and ziprasidone, have relatively limited epidemiological data, but available clinical trial experience with these drugs has not shown an increased risk for diabetes (Table 2).

One possible mechanism for hyperglycemia is impairment of insulin action (i.e., insulin resistance). Drug-induced insulin resistance may occur because of weight gain or a change in body fat distribution or by a direct effect on insulin-sensitive target tissues. Patients treated with olanzapine and clozapine have higher fasting and postprandial insulin levels than patients treated with FGAs, even after adjusting for body weight. To date, studies in humans have not shown adverse effects of any antipsychotic medication on β-cell function, but this issue has not been adequately studied in individuals with psychiatric illnesses.

### Dyslipidemia

An additional related consequence of SGA use is their effect on serum lipids. Although the data are limited, the available evidence suggests that changes in serum lipids are concordant with changes in body weight. Clozapine and olanzapine, which produce the greatest weight gain, are associated with the greatest increases in total cholesterol, LDL cholesterol, and triglycerides and with decreased HDL cholesterol. Aripiprazole and ziprasidone, which are associated with the least amount of weight gain, do not seem to be associated with a worsening of serum lipids. Risperidone and quetiapine appear to have intermediate effects on lipids (Table 2).

### Risk-Benefit Assessment

Despite the adverse effects cited above, a number of factors should be considered when choosing among the antipsychotic medications. These include the nature of the patient's psychiatric condition, specific target signs and symptoms, past history of drug response (both therapeutic and adverse), patient preference, history of treatment adherence, medication effectiveness, psychiatric and medical comorbidities, availability of appropriate formulations (e.g., fast-dissolving oral, short- or long-acting intramuscular), need for special monitoring, and cost of and access to medications. Nonetheless, the risks of obesity, diabetes, and dyslipidemia have considerable clinical implications in this patient population and should also influence drug choice.

Even for those medications associated with an increased risk of metabolic side effects, the benefit to specific patients could outweigh the potential risks. For example, clozapine has unique benefits for treatment-refractory patients and those at significant risk for suicidal behavior. Since treatment response in many psychiatric conditions is heterogeneous and unpredictable, physicians and patients can benefit from the availability of a broad array of different therapeutic agents.

## 4. GIVEN THE ABOVE RISKS, HOW SHOULD PATIENTS BE MONITORED FOR THE DEVELOPMENT OF SIGNIFICANT WEIGHT GAIN, DYSLIPIDEMIA, AND DIABETES, AND HOW SHOULD THEY BE TREATED IF DIABETES DEVELOPS?

Given the serious health risks, patients taking SGAs should receive appropriate baseline screening and ongoing monitoring. Clinicians who prescribe SGAs for patients with psychiatric illnesses should have the capability of determining a patient's height and weight (BMI) and waist circumference. These values should be recorded and tracked for the duration of treatment. Clinicians should also encourage patients to monitor and chart their own weight. It is particularly important to monitor any alteration in weight following a medication change. The patients' psychiatric illness should not discourage clinicians from addressing the metabolic

**Table 3.**
**Monitoring Protocol for Patients on SGAs***

| | Baseline | 4 weeks | 8 weeks | 12 weeks | Quarterly | Annually | Every 5 years |
|---|---|---|---|---|---|---|---|
| Personal/family history | X | | | | | X | |
| Weight (BMI) | X | X | X | X | X | | |
| Waist circumference | X | | | | | X | |
| Blood pressure | X | | | X | | X | |
| Fasting plasma glucose | X | | | X | | X | |
| Fasting lipid profile | X | | | X | | | X |

*More frequent assessments may be warranted based on clinical status

complications for which these patients are at increased risk.

## Baseline Monitoring

The panel recommends that baseline screening measures be obtained before, or as soon as clinically feasible after, the initiation of any antipsychotic medication (Table 3). These include

- Personal and family history of obesity diabetes, dyslipidemia, hypertension, or cardiovascular disease
- Weight and height (so that BMI can be calculated)
- Waist circumference (at the level of the umbilicus)
- Blood pressure
- Fasting plasma glucose
- Fasting lipid profile

These assessments can determine if the patient is overweight (BMI 25.0–29.9) or obese (BMI ≥30), has pre-diabetes (fasting plasma glucose 100–125 mg/dl) or diabetes (fasting plasma glucose ≥126 mg/dl), hypertension (blood pressure >140/90 mmHg), or dyslipidemia. If any of these conditions are identified, appropriate treatment should be initiated. Psychiatrists should not hesitate to refer the patient to the appropriate health care professional or specialist knowledgeable about these disorders.

The panel recommends that nutrition and physical activity counseling be provided for all patients who are overweight or obese, particularly if they are starting treatment with an SGA that is associated with significant weight gain. Referral to a health care professional or program with expertise in weight management may also be appropriate.

Health professionals, patients, family members, and caregivers should be aware of the signs and symptoms of diabetes and especially those associated with the acute decompensation of diabetes such as DKA (Table 4). The latter is a life-threatening condition and always requires immediate treatment. Patients, family members, and caregivers also need to know that treatment with some SGAs may be associated with significant weight gain and a heightened risk of developing diabetes and dyslipidemia. For patients with, or at higher risk for, diabetes and in those treated with other medications that may increase these risks (e.g., valproate, lithium, Depo-Provera), it may be preferable to initiate treatment with an SGA that appears to have a lower propensity for weight gain and glucose intolerance (Table 2). Potential for weight gain should also be considered in the choice of other psychiatric and nonpsychiatric medications.

**Table 4. DKA Clinical Presentation**

Rapid onset of:
- Polyuria, polydipsia
- Weight loss
- Nausea, vomiting
- Dehydration
- Rapid respiration
- Clouding of sensorium, even coma

## Follow-Up Monitoring

The patient's weight should be reassessed at 4, 8, and 12 weeks after initiating or changing SGA therapy and quarterly thereafter at the time of routine visits (Table 3). If a patient gains ≥5% of his or her initial weight at any time during therapy, one should consider switching the SGA. In such a situation, the panel recommends cross-titration to be the safest approach; abrupt discontinuation of an antipsychotic drug should generally be avoided. When switching from one antipsychotic drug to another, it is preferable to discontinue the current medication in a gradual fashion. The profile of the subsequent drug will determine the initial dose and escalation strategy. Particular consideration should be given before discontinuing clozapine because of the potential for serious psychiatric sequelae.

Fasting plasma glucose, lipid levels, and blood pressure should also be assessed 3 months after initiation of antipsychotic medications. Thereafter, blood pressure and plasma glucose values should be obtained annually or more frequently in those who have a higher baseline risk for the development of diabetes or hypertension. In those with a normal lipid profile, repeat testing should be performed at 5-year intervals or more frequently if clinically indicated.

Although limited data are available in children and adolescents regarding the risks of diabetes when SGAs are given, these patients should have their height, in addition to weight, measured at regular intervals and their BMI calculated. BMI percentile adjusted for age and sex should be used to determine if excessive weight gain has occurred, and if present, a change in therapy should be considered.

For people who develop worsening glycemia or dyslipidemia while on antipsychotic therapy, the panel recommends considering switching to an SGA that has not been associated with significant weight gain or diabetes (Table 2). All patients with diabetes should be referred to an American Diabetes Association–recognized diabetes self-management education program, if available. Referral to a clinician with experience treating people with diabetes is recommended. These patients should carry diabetes identification.

Immediate care or consultation is required for patients with symptomatic or severe hyperglycemia (glucose values ≥300 mg/dl), symptomatic hypoglycemia, or glucose levels ≤60 mg/dl, even in the absence of symptoms. The presence of

symptoms of DKA (Table 4), requires immediate evaluation and treatment.

Blood pressure, lipid, and glycemic goals of therapy for people with diabetes apply equally to those who also have psychiatric disorders. However, all goals need to be individualized. The benefits and risks of different therapeutic agents used in the treatment of diabetes and its comorbidities should be considered in the context of the patient's psychiatric condition and treatment.

In summary, the panel recommends the following:

- Consideration of metabolic risks when starting SGAs
- Patient, family, and care giver education
- Baseline screening
- Regular monitoring
- Referral to specialized services, when appropriate

## 5. WHAT RESEARCH IS NEEDED TO BETTER UNDERSTAND THE RELATIONSHIP BETWEEN THESE DRUGS AND SIGNIFICANT WEIGHT GAIN, DYSLIPIDEMIA, AND DIABETES?

Evidence for weight gain and abnormalities of glucose and lipid metabolism in patients taking SGAs is in part derived from case-control studies, pharmacovigilance (e.g., through MedWatch), and database reviews. Many of these studies suffer from their retrospective nature, heterogeneity of methodology, selection or ascertainment bias, and absence of appropriate or well-characterized control subjects. Comparison studies among SGAs are also limited by relatively short periods of study, by failure to control for a possible treatment sequence bias in "switchover" studies, and by not always using clinically equivalent dosages of the medications.

Trials with SGAs should be randomized and controlled, preferably using drug-naïve subjects. Weight gain and measures of glucose and lipid metabolism should be thoroughly evaluated. Study subjects should be well-characterized in terms of their baseline risk factors for diabetes, obesity, and lipid disorders and their degree of baseline impairment in insulin sensitivity and β-cell function. The duration of exposure to the various SGAs should be carefully controlled. Future research studies should focus on the following:

- Baseline body composition in untreated patients with psychiatric disorders and changes that occur during treatment with SGAs need to be better characterized. This would include measures of fat versus fat-free mass and visceral and subcutaneous adipose stores, using valid methods to measure body fat (e.g., magnetic resonance imaging, computed tomography, dual-energy X-ray absorptiometry).
- The contribution of altered neuroendocrine function (e.g., hypothalmic-pituitary-adrenal axis activation) to alterations in body composition and abnormalities in glucose and lipid metabolism needs further study to distinguish the acute effects of stress from the underlying disease process.
- Studies are needed that examine glucose and lipid metabolism as they relate to alterations in insulin sensitivity in peripheral and hepatic tissues (e.g., euglycemic-hyperinsulinemic clamp with labeled glucose infusions), alterations in β-cell function (hyperglycemic clamp or frequently sampled intravenous glucose tolerance test), and alterations in lipid metabolism (using tracer infusions).
- Large prospective studies should be conducted to identify baseline and early treatment factors that predict the later occurrence of abnormalities in body weight and composition and disorders of glucose and lipid metabolism during treatment with these drugs.
- Additional studies are needed to identify whether there are baseline characteristics that predict acute, life-threatening complications (e.g., DKA, pancreatitis).
- Additional data are needed to determine whether the risks of therapy are increased in certain ethnic groups (e.g., African Americans).
- Studies determining the effect of SGAs in various psychiatric disorders are needed to clarify the disease-related risk for the development of weight gain and metabolic disturbances.
- Alterations in energy intake and expenditure as contributors to weight gain in the psychiatric population and how these processes are altered by treatment with SGAs should be studied.
- Studies are needed to determine whether the disorders of body weight and glucose and lipid metabolism are due to central nervous system or peripheral tissue actions of the SGAs. Valuable information on the direct effects of SGAs on different body tissue compartments might be obtained from studies in appropriate animal models.
- Studies of the genetic markers that are associated with, and may be causally related to, the metabolic disturbances occurring in treated patients with psychiatric disorders (e.g., 5-$HT_{2C}$, histamine-H1 receptor alleles) are needed.

**SUMMARY** The SGAs are of great benefit to a wide variety of people with psychiatric disorders. As with all drugs, SGAs are associated with undesirable side effects. One constellation of adverse effects is an increased risk for obesity, diabetes, and dyslipidemia. The etiology of the increased risk for metabolic abnormalities is uncertain, but their prevalence seems correlated to an increase in body weight often seen in patients taking an SGA. Direct drug effects on β-cell function and insulin action could also be involved, since there is insufficient information to rule out this possibility. In the general population, being overweight or obese also carries a much higher risk of diabetes and dyslipidemia.

These three adverse conditions are closely linked, and their prevalence appears to differ depending on the SGA used. Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine appear to have intermediate effects. Aripiprozole and ziprasidone are associated with little or no significant weight gain, diabetes, or dyslipidemia, although they have not been used as extensively as the other agents.

The choice of SGA for a specific patient depends on many factors. The likelihood of developing severe metabolic disease should also be an important consideration. When prescribing an SGA, a commitment to baseline screening and follow-up monitoring is essential in order to mitigate the likelihood of developing CVD, diabetes, or other diabetes complications.

## APPENDIX

### Consensus Panel

Eugene Barrett, MD, PhD, Chair; Lawrence Blonde, MD, Stephen Clement, MD, John Davis, MD, John Devlin, MD, John Kane, MD, Samuel Klein, MD, William Torrey, MD.


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### Presenters at the Conference

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